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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,562	03/06/2007	Tony George	Y0087.70013US01	4715

23628 7590 01/12/2010

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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1627	

MAIL DATE	DELIVERY MODE
01/12/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,562	GEORGE ET AL.	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-27,29-35 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-27, 29-35, and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/29/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

This Office Action is in response to the amendment submitted on 10/07/09. Claims 25-27, 29-35, and 37 are currently pending in the application, with claims 1-24, 28, and 36 having being cancelled. Accordingly, claims 25-27, 29-35, and 37 are being examined on the merits herein.

Receipt of the aforementioned amended claims and Information Disclosure Statement (IDS) is acknowledged and has been entered.

Applicant's argument with respect to the rejection of claims 1-8 over Popik in view of Fava (erroneously labeled as Shytle) has been fully considered. Given that applicant has amended the claims, such rejection is now moot. Consequently, the rejection of claims 1-8 under 35 U.S.C. 103(a) over Popik in view of Fava (erroneously labeled as Shytle) is hereby withdrawn.

1. Applicant's argument that the amended claims 29-35 are patentable over Popik in view of Fava and in further view of Shytle has been fully considered but is not found persuasive. The Examiner respectfully points out that applicant is arguing the amended claims and features not previously presented. It is noted that the features upon which applicant relies (i.e., treatment of major depressive disorder that is single episode or recurrent episode major depressing disorder and/or adjunctive treatment of major

depressive disorder) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). As a result, the Examiner contends that such arguments are moot. Consequently, the Examiner maintains that the rejection of claims 1-8 and 25-36 over Popik in view of Fava and in further view of Shytle was indeed proper.

For the foregoing reasons, the rejections of claims 1-8 over Popik in view of Fava is hereby withdrawn. The rejection of claims 1-8 and 25-36 over Popik in view of Fava and in further view of Shytle was indeed proper. However, in view of applicant's amendment and cancellation of claims 1-8, the following 112, first paragraph and modified 103 (a) Final rejections are being made.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-27, 29-35, and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As stated by the court in Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004), regarding the written description requirement:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described.

In this instant application, applicant did not specifically describe adjunctively treating major depressive disorder comprising exo-S-mecamylamine and additional agents. Because adjunctively treating major depressive disorder entails assisting of a primary therapy of major depressive disorder and given that applicant did not disclose the method of treating major depressive disorder as an adjunct therapy, the Examiner contends that one skill in the art would not be able to readily envisage that applicant was indeed in possession of adjunctively treating major depressive disorder. Consequently, due to this lack of written description, the Examiner contends that the specification did not reasonably convey to those skilled in the art that the applicant was in possession of such limitation as of the date of invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25, 27, 29-35, and 37 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Popik et al. (British Journal of Pharmacology, 2003, Vol. 139, pgs. 1196-1202, previously cited) in view of Fava (Biological Psychiatry, 2003, Vol. 53, pgs. 649-659) in view of Shytle et al. (U.S. 6,734,215 B2, previously cited).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Popik et al. teach that epidemiological and clinical observations suggest the involvement of nicotinic acetylcholine receptors (nAchRs) in depressive illness (see abstract, section 1). In fact, lines of evidence indicate that nAChRs are involved in major depression (a.k.a. major depressive disorder; see pg. 1196, left col., Introduction, paragraph 2 and right col., paragraph 2). Thus, Popik et al. sought to determine if nAChRs antagonists produce antidepressant like effects (i.e. AD; see pg. 1197, left col.,

paragraph 3). In his study, Popik et al. investigated if the nAChR antagonist, mecamylamine or MEC, produced and/or influenced AD-like effects of citalopram (see pg. 1197, left col., last paragraph). Particularly, Popik et al. demonstrated that co-treatment of 2 mg/kg of body weight of citalopram (i.e. CIT) and 2.5 mg of mecamylamine (i.e. MEC) significantly inhibited the immobility in the tail-suspension test (instant claims 29 and 33-34; see pg. 1199, left col., paragraph 2 and abstract) suggesting a positive effect on the depression. Importantly, Popik et al. demonstrated that the interaction between nAChR antagonists and CIT appeared to produce a synergistic effect (see abstract and pg. 1200, right col., last paragraph).

Popik et al. do not specifically teach a method of adjunctively treating refractory major depression or refractory major depressive disorder. Similarly, Popik et al. do not teach administration or oral administration of exo-S-mecamylamine that is substantially free of exo-R-mecamylamine.

While Popik et al. teach sequential administration of MEC and CIT to mice, Popik et al. also indicated that the tail-suspension test is typically used to test anti-depressant effects (see pg. 1197, last paragraph). Moreover, it would be well within the purview of the skilled artisan to formulate MEC in the same formulation (i.e. together) as CIT since Popik et al. demonstrated that both MEC and CIT act in a synergistic manner. Moreover, the Examiner contends that it would have been obvious to one of ordinary

skill in the art to administer the therapy of Popik as a second line of therapy (i.e. adjunct treatment) if the desire is to enhance the treatment of major depressive disorder.

Fava is being provided to demonstrate that unipolar depressive disorders (i.e. major depression or major depressive disorder) entails treatment resistant depression (i.e. refractory major depression) and is characterized by the occurrence of an inadequate response following adequate antidepressant therapy among such patients and consequently such patients fail to achieve remission (see pg. 649, left col., Introduction and abstract). Fava further teach that such depression also include the types of depression that are non-responsive as well wherein the goal for such depression should be complete remission (see pg. 649, left col., Introduction and abstract). Thus, the Examiner contends that to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the method of Popik et al. to treat refractory patients of major depression since Fava teaches that major depression entails resistant major depression patients who are non-responsive to adequate antidepressant therapy and Popik demonstrated effective treatment of major depression.

Shytle et al. teach the use of exo-S-mecamylamine or a pharmaceutically acceptable carrier salt thereof, substantially free of its exo-R-mecamylamine, said amount being sufficient to ameliorate neuropsychiatric disorders including depression (instant claims 25; see abstract, col. 5, lines 16-22, and col. 9, lines 29-38). Shytle et al.

further teach that the aforementioned formulation for improved therapy with fewer side effects and for improved medical compliance, quality of life and social functioning (see col. 5, lines 25-32). Particularly, Shytle et al. teach that the pharmaceutical composition include a therapeutically effective of exo-S-mecamylamine or its pharmaceutically acceptable salt with a carrier as an oral or parenteral formulation in an amount of about 0.5 mg to about 1000 mg (instant claims 30-31 and 37; see col. 5, lines 33-67; col. 6, lines 1-11; and col. 9, lines 39-64). Shytle et al. further teach that the formulation can be administered one to four times per day (instant claim 32; see col. 24, claims 7-11).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to substitute the exo-S-mecamylamine of Shytle et al. into the method of Popik et al. and administer the combination of exo-S-MEC with CIT to refractory patients with major depressive disorder since Fava teaches that major depression or major depressive disorder entails resistant-major depression patients who are non-responsive to adequate antidepressant therapy and given that Shytle et al. teach that the exo-S-MEC possess fewer side effects and help in achieving patient compliance. Moreover, one of ordinary skill in the art would have found it obvious to administer the method of Popik adjunctively to patients since Popik demonstrated that its method was effective in treating depression and if the desire of one skilled in the art is to enhance the efficacy of such treatment. Thus, given the teachings of Shytle, Popik, and Fava, one of ordinary skill would have been motivated to substitute exo-S- mecamylamine for the mecamylamine of Popik et al. and further combined it with citalopram and

administer the formulation to refractory major depressive disorder patients with the reasonable expectation of providing a method with fewer side effects that is effective in treating such subset of major depressive disorder patients and a method that helps in improving patient compliance.

Popik et al. do not disclose the exact dosage of Citalopram (CIT) as applicant. However, Popik et al. do teach CIT at a dosage of 2mg/kg of body weight. Consequently, it is well within the purview of the skill of the artisan at the time of the invention to adjust the dosage of CIT depending on the patient to be treated during the course of routine experimentation so as to obtain the most effective CIT dosage.

While the exact dosage of CIT is not disclosed by Popik et al., it is generally noted that differences in dosages do not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or dosage is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Given that applicant did not point out the criticality of specific ranges or dosages of the invention, it is concluded that the normal desire of scientists or artisans to improve upon what is already generally known would provide the motivation to determine where in a disclosed set of ranges is the optimum combination of dosages.

Claim 26 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Popik et al. (British Journal of Pharmacology, 2003, Vol. 139, pgs. 1196-1202, previously cited) in view of Fava (Biological Psychiatry, 2003, Vol. 53, pgs. 649-659) in view of Shytle et al. (U.S. 6,734,215 B2, previously cited) as applied to claims 25, 27, 29-35, and 37 and in further view of Cassano et al. (Eur. Arch. Psychiatry Clin. Neurosci. 1993, Vol. 242, pgs. 373-380).

The Popik, Fava and Shytle references are as discussed above and incorporated by reference herein. However, Popik, Fava, and Shytle do not teach the method of treating single major depressive disorder or recurrent major depressive disorder.

Cassano et al. teach that out 687 patients with primary major depressive disorder (MDE), 213 or 31% were categorized as single episode (pg. 373, abstract). Additionally, Cassano et al. teach that while most depressive disorders recur, there is a minority of patients (i.e. one out of three) do not progress beyond the single episode (see pg. 373, left col.). Additionally, Cassano et al. teach that patients with recurrent major depressive disorder tend to have some familial causation or association. Importantly, Cassano et al. teach that single episode MDE is less severe than recurrent episode and that single episode major depressive disorder is an illness of shorter duration as compared to recurrent episode MDE (see Discussion Section, pg. 377, right col., Section of Role of Age at Onset in Subclassifying SE).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to try the modified method of Popik in patients of single episode major depressive disorder since Cassano et al. teach that such disorder does not last long and is less severe as compared to other major depressive disorders and thus one of ordinary skill in the art would have had a reasonable expectation that such method will be successful in alleviating such patients' illness. Thus, given the teachings of Popik, Fava, Shytle, and Cassano, one of ordinary skill would have been motivated to utilize the method of Popik in treating single episode major depressive disorder with the reasonable expectation of providing a method that is effective in treating such subset of major depressive disorder patients and a method that helps in quickly alleviating the disease.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1627

01/07/2010

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627